In substantive Response to the *Ex parte Quayle* Office Action from the Examiner in charge of the above-identified application and the Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures, as mailed April 20, 2004 and extended through July 20, 2004, applicants hereby amend the Specification of the above-identified application pursuant to 37 C.F.R. 121.

Such amendment is being made by submission of replacement amended paragraph pages for the Specification for the changes listed below. A clean copy version and a marked-up copy version of the replacement amended paragraph pages for the Specification are enclosed as separate documents.

In the Specification:

Amend the Specification text appearing at:

Page 14, lines 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23 respectively; and

Page 15, line 2.

In addition, pursuant to and in compliance with the requirements of 37 C.F.R. 1.821-1.825, applicants also enclose herewith a third paper form copy of the "Sequence Listing" containing disclosures of nucleotide sequences and/or amino acid sequences. Applicants respectfully request and direct that the enclosed third paper form copy of the "Sequence Listing" containing

disclosures of nucleotide sequences and/or amino acid sequences be formally entered into and be made officially of record for the Specification of the above-identified application.

Applicants ' undersigned attorney also declares and verifies that this amendment and requested formal entry of the third "Sequence Listing" in paper form copy is proper and correct in all respects; and that the enclosed third "Sequence Listing" in paper copy form is completely supported by the descriptive content and enabling disclosure of the Specification text originally filed September 2, 1998 as USSN 09/145,916

Furthermore, applicants' undersigned attorney also declares and verifies that the enclosed "Sequence Listing" submitted in paper form copy does not contain or include any New Matter; and that the submission of a third computer readable form (CRF) copy of the "Sequence Listing" is also provided, the third computer readable form (CRF) copy being identical in substantive content to the enclosed third paper form copy.

Accordingly, this third paper form copy "Sequence Listing" is to be formally entered into and made part of the Specification; and the formally entered third paper form copy "Sequence Listings" shall now constitute part of the Specification during the substantive prosecution of this application.

Respectfully submitted,

MICHAEL SIMONS
RUDIGER VOLK
ARIE HOROWITZ

Date: July 19, 2004

By: David Prashker

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS	: Simons *et al.*
SERIAL NO.	: 09/145,916
FILED	: September 2, 1998
FOR	: "STIMULATION OF ANGIOGENESIS VIA ENHANCED ENDOTHELIAL EXPRESSION OF SYNDECAN-4 CORE PROTEINS"
EXAMINER	: David Guzo
GROUP ART UNIT	: 1636
ATTORNEY'S DOCKET NO.	: BIS-039

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Commission for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on: July 19, 2004

Attorney for applicants: David Prashker

Signature: [signature]

Date: July 19, 2004

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CLEAN COPY VERSION OF AMENDED SPECIFICATION SUBMITTED
PURSUANT TO 37 C.F.R.1.121(b)(1)(ii)

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

Applicants, in fulfillment of and in accordance with the requirements of 37 C.R.F. 1.121(b)(1)(ii), hereby submit a clean copy

version of the present amendments to the Specification which appear at the following location:

Page 14, lines 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23 respectively; and

Page 15, line 2.

Respectfully submitted,

MICHAEL SIMONS
RUDIGER VOLK
ARIE HOROWITZ

Date: July 19, 2004

By: David Prashker

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Registration No. 29,693
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Fig. 1 is a representation of a prepared DNA sequence fragment;

Fig. 2 is a recitation of the DNA sequence coding for the extracellular domain of syndecan-1 [SEQ ID NO:1];

Fig. 3 is a recitation of the DNA sequence coding for extracellular domain of syndecan-2 [SEQ ID NOS:2 & 3];

Fig. 4 is a recitation of the DNA sequence coding for the extracellular domain of syndecan-3 [SEQ ID NO:4];

Fig. 5 is a recitation of the DNA sequence coding for the extracellular domain of syndecan-4 [SEQ ID NO:5];

Fig. 6 is a recitation of the DNA sequence coding for the extracellular domain of glypican- 1 [SEQ ID NOS:6 & 7];

Fig. 7 is a recitation of the DNA sequence coding for the transmembrane domain of syndecan-1 [SEQ ID NO:8];

Fig. 8 is a recitation of the DNA sequence coding for the transmembrane domain of syndecan-2 [SEQ ID NOS:9 & 10];

Fig. 9 is a recitation of the DNA sequence coding for the transmembrane domain of syndecan-3 [SEQ ID NO:11];

Fig. 10 is a recitation of the DNA sequence coding for the transmembrane domain of syndecan-4 [SEQ ID NO:12];

Fig. 11 is a recitation of the DNA sequence coding for the transmembrane domain of GP1 [SEQ ID NOS:13 & 14];

Fig. 12 is a recitation of the DNA sequence coding for the transmembrane domain of perlecan [SEQ ID NO:15];

Fig. 13 is a recitation of the DNA sequence coding for the cytoplasmic domain of syndecan-4 [SEQ ID NO:16];

Fig. 14 is a graph illustrating the in-vitro growth assays of ECV-derived cell clones;

Figs. 15A-15C are photographs showing the results of Matrigel growths assays;

Fig. 16 is a graph illustrating the effect of syndecan construct expression on endothelial cell migration in Boyden chamber assays;

Figs. 17A-17F are photographs showing BudR uptake in opiop homozygous *(-/-)* and heterozygous *(+1-)* mice;

Fig. 18 is a photograph showing Northern blot analysis of gene expression in PR-39 transgenic mice; and

Fig. 19 is a graph illustrating in-vitro microvascular reactivity in PR-39 transgenic mice.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides both the tangible means and the methods for causing an overexpression of extracellular, heparan sulfate carrying, proteoglycans on-demand at and through the surface of endothelial cells; and via such on-demand overexpression of proteoglycans to stimulate angiogenesis in-situ. The tangible means include a prepared DNA segment comprising sequences coding for an extracellular domain, a transmembrane domain, and the cytoplasmic domain of the